Techniques in Vascular and Interventional Radiology

Radiation Segmentectomy and Radiation Lobectomy: A Practical Review of Techniques

Anuj Malhotra, MD,* David M. Liu, MD,† and Adam D. Talenfeld, MD, MS*

The radiation segmentectomy technique may be defined as the administration of transarterial radioembolization delivered to 1 or 2 hepatic segments with the intention of segmental tissue ablation. Since first being described in 2011, radiation segmentectomy has quickly gained acceptance as a safe, effective, and potentially curative outpatient treatment for selected lower stage hepatocellular carcinomas. We describe our recommended techniques for radiation segmentectomy with glass or resin radiomicrospheres, including patient selection, dosimetry, microcatheter techniques, and clinical and imaging follow-up, accompanied by a brief review of the radiation segmentectomy literature. Radiation lobectomy, defined as the ablation of an entire hepatic lobe via transarterial radioembolization, is an area of growing interest in many centers. We also review the existing radiation lobectomy literature and suggest which patient and tumor factors may be associated with higher likelihood of successful treatment.

Tech Vasc Interventional Rad 22:49-57 © 2019 Elsevier Inc. All rights reserved.

KEYWORDS Radiation segmentectomy, Segmental radioembolization, Y90 segmentectomy, Radiation lobectomy, Y90 lobectomy

Introduction

Radiation segmentectomy (RS) (segmental transarterial radioembolization using intentionally ablative doses of yttrium-90 radiomicrospheres) was first described as an alternative treatment for focal hepatocellular carcinoma (HCC) in 2011 by Riaz et al.[1] In a case series of 84 patients with tumors receiving arterial supply from only 1 or 2 segments, they administered entire lobar doses of glass radiomicrospheres via these segmental arteries, essentially sparing the remaining ipsilateral segments any radiation toxicity while delivering a median dose of 521 Gy to the treated segments utilizing glass microspheres (TheraSphere, BTG Interventional Medicine; London, United Kingdom). Toxicities were reported to be low or lower than had previously been described for conventional lobar radioembolization.

Early evidence that RS can be a truly ablative technique came from a study of 33 postradiation segmentectomy explants from liver transplant patients with solitary HCCs <5 cm diameter.[2] With a median of 242 Gy delivered to these segments, the investigators found 90%-100% tumor necrosis in all explants, also with glass microspheres.

With highly promising early results, RS is becoming part of standard practice at an increasing number of centers offering radioembolization. To our knowledge, all published RS studies to-date have utilized glass radiomicrospheres to treat HCC; however, some practitioners do use resin radiomicrospheres to achieve what are anecdotally noted to be similar results[3] (Kierans, et al abstract of case series World Conference on Interventional Oncology, 2016).

Radiation lobectomy (RL) is a similar technique with the intent to develop marked ipsilateral lobar atrophy, resulting in the management of potential microvascular and macrovascular spread of disease with the reported potential benefit of eliciting contralateral lobe hypertrophy after unilateral lobar TARE. RL may hold promise as an alternative to portal vein

*Division of Interventional Radiology, Department of Radiology, Weill Cornell Medicine/NewYork-Presbyterian Hospital, New York, NY.
†Angio/Interventional Radiology Section, Department of Radiology, University of British Columbia/Vancouver General Hospital, Vancouver, BC, Canada.
Address reprint requests to Division of Interventional Radiology, 525 E. 68th Street, Payson 508, New York, NY 10536.
E-mail: adt9010@med.cornell.edu

1089-2516/14/$-see front matter © 2019 Elsevier Inc. All rights reserved.
https://doi.org/10.1053/j.tvir.2019.02.003

embolization for some well-selected patients and as destination therapy for others; however, no intent to treat study examining dose modulation or optimization has yet been conducted. RS and RL will be discussed in separate sections of this review.

Radiation Segmentectomy

Indication/Clinical Evaluation

Radiation segmentectomy represents off-label use for both commercially available products. Patients treated with RS at the authors' institutions are frequently referred for treatment based on consensus recommendation by an multidisciplinary hepatobiliary tumor board, with input from interventional radiology, hepatobiliary transplantation surgery, surgical oncology, medical oncology, radiation oncology, and hepatology specialists. Patients may be poor candidates for surgical resection due to portal hypertension or other comorbid disease, or they may be undergoing evaluation for liver transplantation. Patients will usually be poor candidates for percutaneous thermal ablation due to comorbidities raising the risk of general anesthesia, larger tumor size, or unfavorable tumor location, such as in the dome of the liver, or near the gallbladder, bowel or porta hepatis (Figs. 1 and 2). Patients most often have primary liver cancer but can also have oligometastatic disease confined to 1 or 2 segments.

As with all candidates for radioembolization, patients are seen in consultation in advance of mapping angiography.

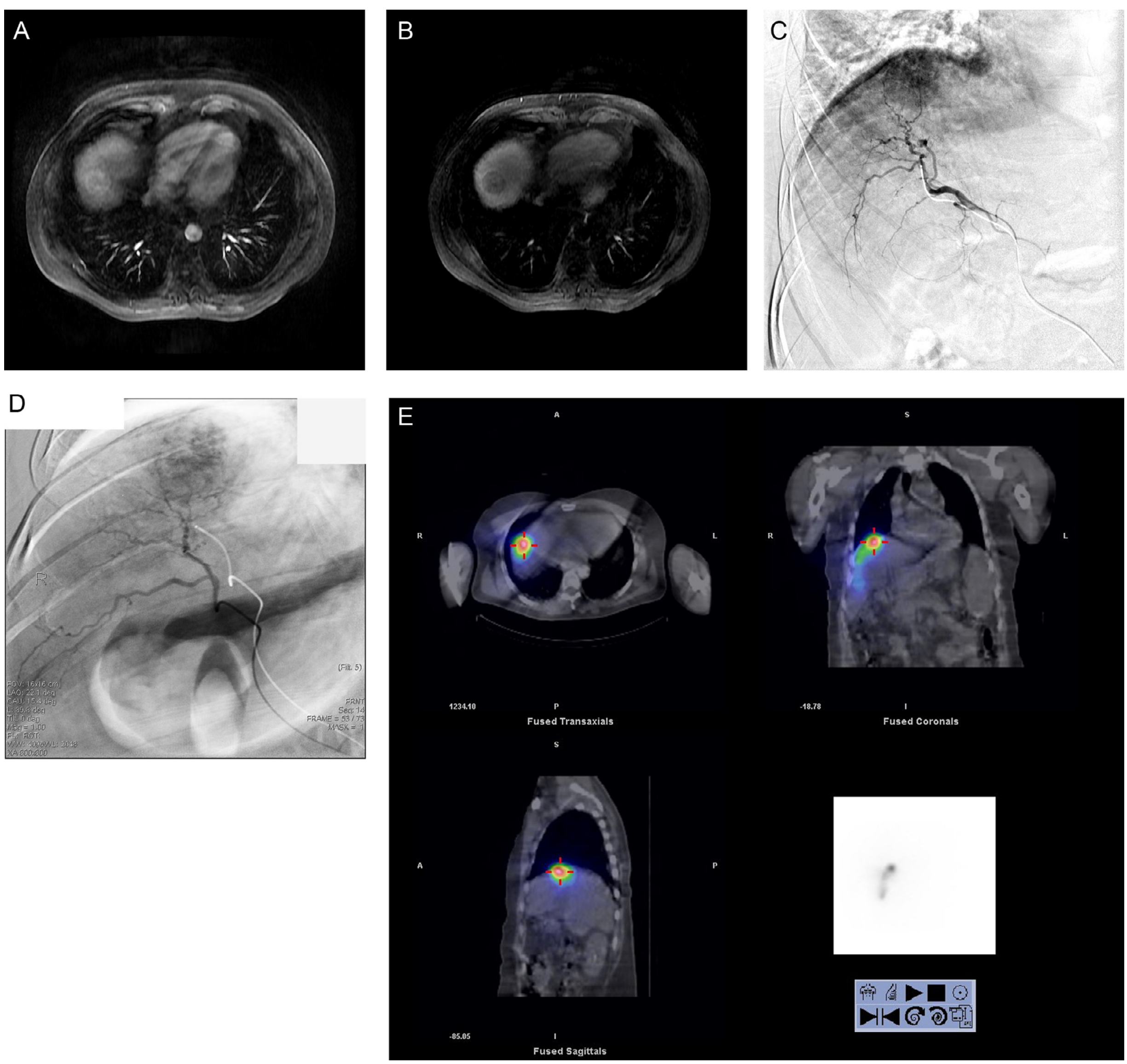

Figure 1 Typical radiation segmentectomy target lesion appearance and treatment images. A. An arterial phase axial postcontrast MR image shows a 3.2 cm diameter enhancing HCC in the hepatic dome. B. Portal phase MR image shows washout and pseudocapsule. C. Digitally subtracted angiography (DSA) shows tumor blush in the dome arising from the anterior division of the right hepatic artery. D. Segmental DSA from treatment position. E. Multiplanar single positron emission computed tomography (SPECT) images confirm intense radiotracer uptake by tumor and minimal or no radiation exposure to most of the liver.

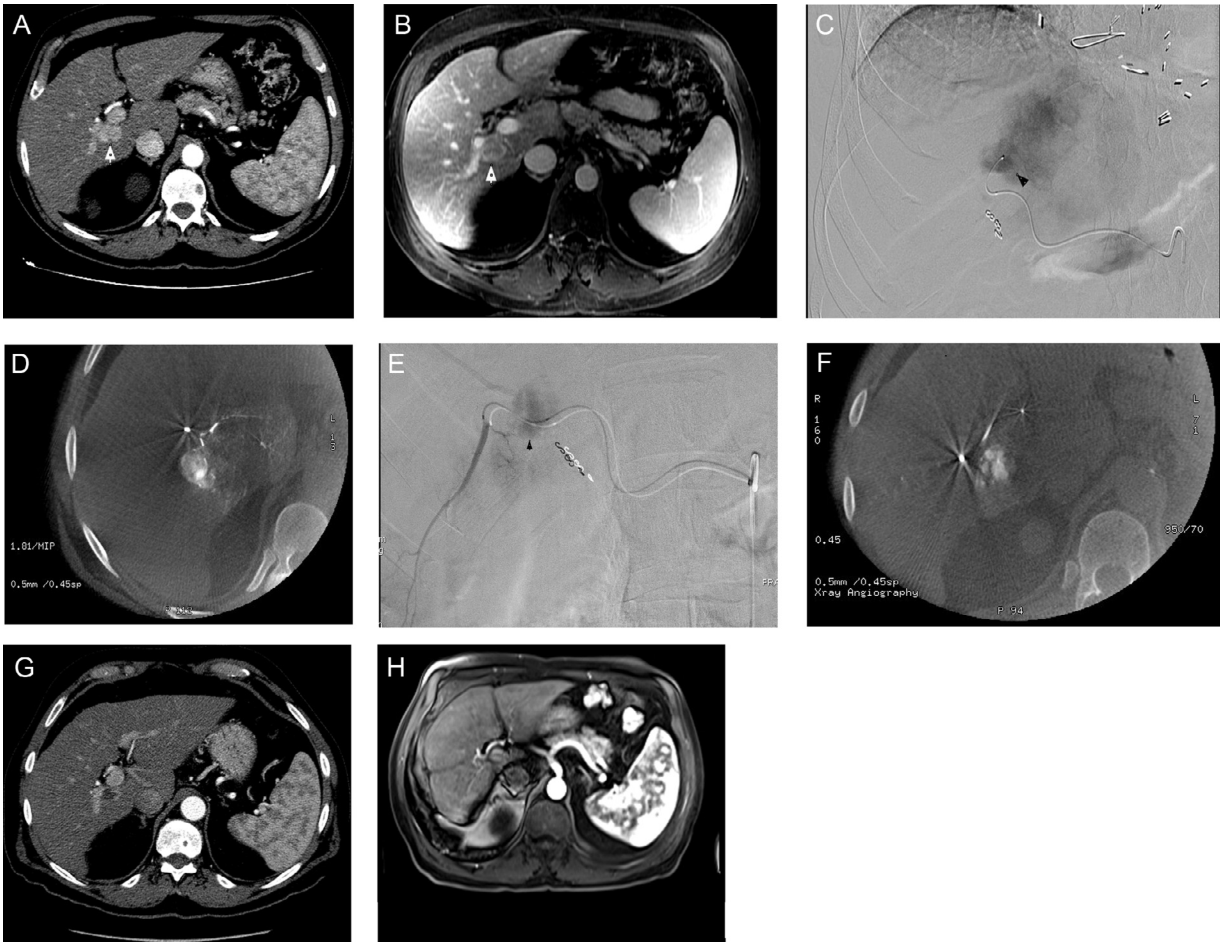

Figure 2 Radiation segmentectomy of periportal HCC. A. Arterial phase CT shows a 2.4 cm diameter hepatoma on the margin of segments 1 and 6 (white arrowhead), abutting main and posterior right portal vein segments. B. Portal phase MR shows the HCC (white arrowhead) with central washout. C. DSA with curve-tipped microcatheter in the caudate artery, subtle tumor blush is seen at the inferolateral margin of the segment (black arrowhead). D. Axial contrast CBCT image from same location clearly demonstrates the tumor. E and F. DSA with the microcatheter positioned in segment 6 also shows tumor blush (black arrowhead), and CBCT confirms. Periportal and other central tumors will frequently recruit blood supply from multiple small arteries, sometimes precluding treatment. G. One month post-RS arterial phase CT shows a rind of enhancing granulation tissue around necrotic, nonenhancing tissue. H. Fourty-two months post-RS, the tumor has disappeared and the caudate lobe is atrophic. The most heavily treated portion of segment 6 is also atrophic, leaving a nonenhancing linear scar. The patient later died of metastatic prostate carcinoma. His HCC never recurred.

We aim to ensure all patients receive liver protocol MRI or CT, CBC, PT/INR, LFTs, basic metabolic panel, and tumor markers such as alpha fetoprotein, carcinoembryonic antigen (CEA), and/or cancer antigen (CA) 19-9 within 30 days of the planned treatment. Patients with Child-Pugh B cirrhosis or ECOG performance status of 2 are counseled that RS, like any transarterial therapy, carries a risk of hepatic decompensation. We do not typically offer radiation segmentectomy to patients with Child C cirrhosis or ECOG PS >2.

Dosimetry

Noting complete necrosis in 14 of 21 patients receiving >190 Gy vs only 3 of 12 patients receiving <190 Gy in their explant study using glass radiomicrospheres, Vouche et al recommended a 190-200 Gy dose target utilizing a two compartment (liver and lung) Medical Imaging Radiation Dose (MIRD) model, as had an earlier dose-escalation study performed with lobar administration.[2,4] With glass radiomicrospheres, a 3, 5, or 7 GBq dose vial is typically used to achieve this target dose.

We have also successfully used a 200 Gy MIRD dosimetry target for RS with resin microspheres, though a lower target dose may likely be adequate with resin. Since the maximum tolerable dose to cirrhotic liver has been established at 70 Gy, some providers use the partition model to target as low as 70 Gy to nontumor parenchyma within the segment when treating HCC with RS.[3] The DAVYR app (University of British Columbia, Vancouver, BC, available free for iOS devices) is useful in calculating, body surface area (BSA), MIRD and partition-based dosimetry and for comparing prescribed activity between each of the three dosimetric models.

In its dosimetric recommendations for segmentectomy with resin microspheres, an expert panel in 2012 suggested simply prescribing enough activity to allow embolization to stasis.[3] We have also safely used this technique, though our delivered dose in 1 case achieved 485 Gy utilizing resin microspheres. Since it is possible that doses well exceeding 200 Gy may risk local adverse events, such as bilomas, without necessarily improving treatment response, we recommend remaining at or below the 200 Gy MIRD target for the segmental volume, or lower if using partition. Obtaining cone beam CT (CBCT) angiogram images of the target volumes during mapping will greatly facilitate accurate dosimetry.

Angiographic Technique

Because radiation segmentectomy typically leads to radiation necrosis of the entire treated volume, a principal aim during mapping angiography is to position the microcatheter as distally as possible while still ensuring the treatment zone will encompass the entirety of the targeted tumor. Microcatheter techniques useful in selecting distal hepatic artery branches are described elsewhere in this edition. Digitally subtracted angiography (DSA) and CBCT angiography are routinely performed from the proper hepatic or lobar artery to allow for prompt identification of the number and locations of arterial branches supplying the target tumor(s). Coil embolization of hepatic-extrahepatic collateral arteries is usually unnecessary, since microcatheter positioning is routinely well distal to these branches. Still, care should always be taken to identify any branches that could lead to nontarget embolization, such as a falciform artery arising from the left hepatic.

Once the targeted segmental or divisional artery is selected, DSA and CBCT angiography are repeated. With either radioembolic, one should evaluate the pattern of reflux from the target artery into proximal and adjacent arterial branches using high quality DSA during mapping. Beyond identifying target and nontarget branches, a close review of DSA images will inform an appropriate flow rate and x-ray delay for best CBCT image acquisition.

Comparing target vessel CBCT with lobar or proper hepatic CBCT allows for easy confirmation of complete tumor coverage and provides reference volumes for subsequent dosimetry. It is important to carefully inspect treatment volume margins for adequacy of tumor coverage, especially when treating tumors along the watershed between segments or lobes (Figs. 2 and 3). When tumor arterial supply arises from more than 2 segmental branches, or in order to spare hepatic tissue from ablation, coil embolization of branches supplying

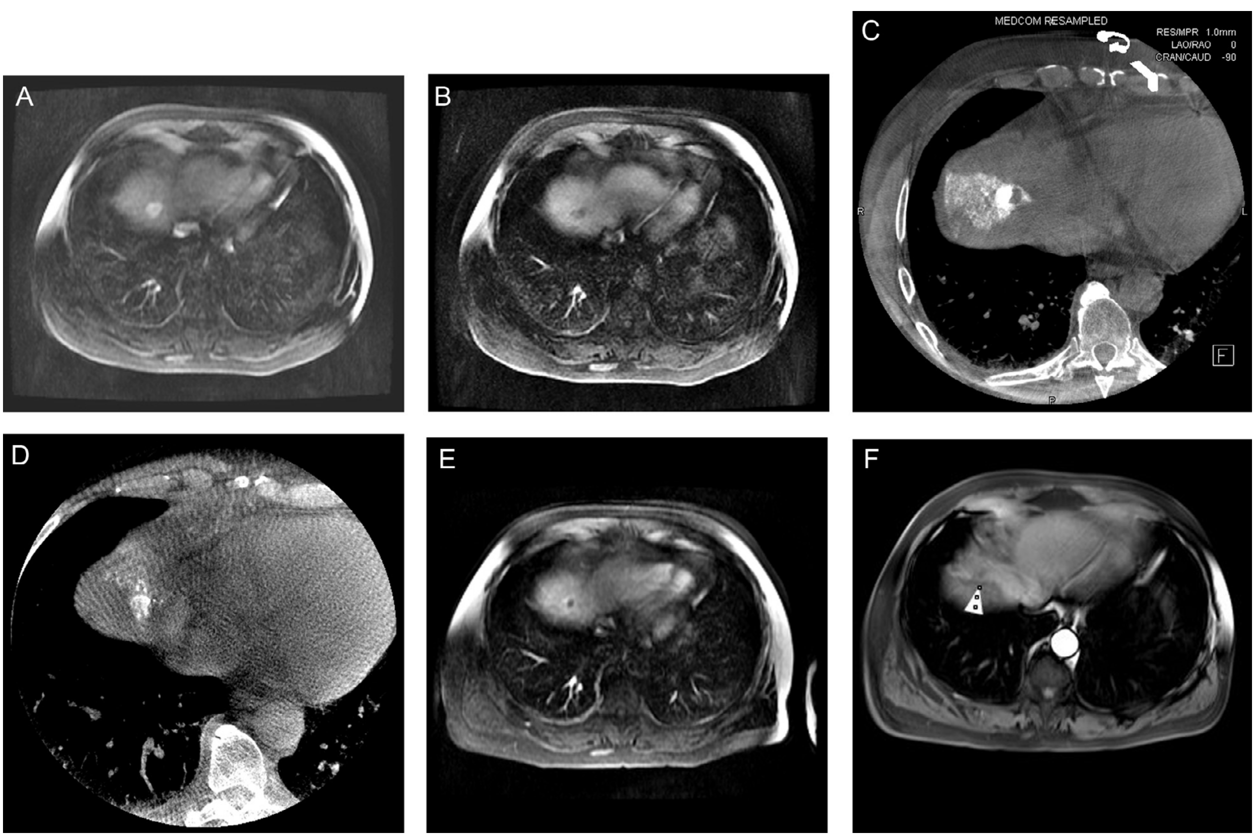

Figure 3 RS of segment 4/8 watershed HCC. A and B. Arterial and portal phase MR images show the 2.1 cm diameter tumor along the margin of segments 4a and 8 in the hepatic dome. C. Contrast CBCT image from a branch of segment 8 shows the target tumor. Enhancement medial to the tumor is contrast in an adjacent hepatic vein tributary. Between the vein and enhancing tumor is a region of non-enhancing tumor tissue. D. CBCT image from a branch of segment 4a shows additional supply to the tumor corresponding to the region of non-enhancement seen in C. E. Arterial phase postcontrast MRI 1-month post-RS shows tumor necrosis (dark center) and rim of granulation tissue, the hyperenhancement of which persisted through venous phases (not shown). F. Arterial phase MRI 51 months post-RS shows a faint cavity representing the treated tumor (white arrowhead) surrounded by a band of hyperenhancing granulation tissue at the margins of the atrophic treated tissue.

relatively less tumor territory can be performed to redistribute flow to remaining tumor branches.[5] For example, the segment 4 branch may be coil embolized in order to redirect flow to segment 5 or 8 branches.

Although most of the prescribed glass microspheres should be delivered well before the complete 20 mL of normal saline have been injected, if there is concern about glass microsphere delivery outside the target volume due to reflux, such as in the case of a particularly small target volume and/or a relatively hypovascular tumor, flow dynamics during treatment infusion can be simulated by performing DSA at a rate of 0.5 mL/sec for 20 mL using a 10 seconds x-ray delay and a 1 frame/sec exposure.

Delivery

With glass microspheres, delivery technique is identical to that used for lobar infusion.

With resin microsphere delivery, close attention should be paid to fluoroscopic images of contrast injection between radiomicrosphere aliquots throughout treatment. It is important when performing segmentectomy using resin radiomicrospheres to recognize initial slowing of forward flow in the treated subsegmental and segmental branches and to reduce the size of infused radiomicrosphere aliquots accordingly. Although slowing and stasis may occur with resin segmentectomy, if no slowing occurs, treatment proceeds in identical fashion to as during lobar infusion, “going to air” prior to catheter removal.

If sluggish antegrade flow is noted, pausing treatment for 1-2 minutes will often allow delivered spheres to settle more distally, enabling infusion of 1 or more additional small aliquots, similar to techniques used in uterine artery embolization. Reflux of a small amount of spheres from a target segment into an adjacent hepatic segment is likely to be of little clinical consequence; however, continuing to load larger aliquots of spheres despite slowing of flow unnecessarily risks nontarget delivery during microcatheter flushing or upon catheter removal. Therefore, if obvious slowing of forward flow recurs or persists after a 1-2 minute pause in treatment, the microcatheter should be flushed three times with 20 mL syringes of dextrose 50% water (D5W) prior to removal according to standard operating procedure.

Clinical and Imaging Follow-Up

Patients should be counseled that they may likely feel fatigue and mild-to-moderate pain in their abdomen, back and/or shoulder, depending on the segment(s) being treated, which can be worse with deep breathing. Patients are advised that these symptoms typically peak 2-3 days after treatment, last up to a week, and may be accompanied by nausea or lack of appetite. As with other radioembolization patients, we prescribe a tapered methylprednisolone dose pack to reduce fatigue and nausea unless contraindicated by diabetes. We also routinely prescribe ondansetron for nausea and a short course of opioid pain medication and stool softeners. We stress to patients the importance of staying hydrated by drinking 6-8 cups of water daily.

Patients are instructed to return for an office visit 1 week after treatment, at which time a focused history and physical is performed and bloodwork is ordered if indicated. We usually obtain a liver protocol MRI 1 month post-treatment, which, we counsel patients, we consider a new baseline scan. Although we often see treatment response at the 1-month scan, we explain to our patients that we order this scan as a way to identify the development of any new tumors outside the segmentectomy zone, and we do not necessarily expect to see treatment effect this early. Some providers opt to skip the 1-month scan and obtain first follow-up imaging at 3 months.

A new complete set of labs is ordered to coincide with the 1 month post-treatment scan and every subsequent scan, which we obtain at 3-month intervals in coordination with the referring hepatologist or medical oncologist. For patients with primary liver cancer, we revert to q6 month imaging once we confirm no new disease for 12 months after treatment.

Expected Outcomes

Imaging findings typical of radiation segmentectomy after 3-6 months include wedge-shaped enhancement throughout the treatment zone that persists from arterial through venous phases[6] (Fig. 4). These features should not be confused with progression of hypervascular disease. Markedly hypervascular target tumors will frequently demonstrate complete lack of internal enhancement even at the initial 1-month post-treatment scan; though persistence of internal enhancement at 1 month should not be misinterpreted as treatment failure. A thin rim of arterial enhancement at the margin of the treated tumor which persists through the venous phases is also a normal sign of post-treatment change, as are scattered foci of non-enhancement surrounding the tumor, consistent with radiation necrosis within the treated segment. At subsequent follow-up, it is common for both the tumor and the surrounding treated nontumor tissue to involute, with a characteristic wedge-shaped retraction of the hepatic capsule (Fig. 4).

Early data suggest radiation segmentectomy for early stage HCC has the potential to be a truly ablative technique, with very low rates of local disease progression. A study of explant pathology from 33 previously treatment-naïve glass RS patients with HCCs 5 cm or smaller not amenable to resection or percutaneous ablation showed >90% pathology-proven necrosis in all patients and 100% necrosis in 17 patients (52%).[2] With a median follow-up of 27 months, time-to-progression was 33 months and overall survival was 53 months.

Recently, 40 radiation segmentectomy patients were propensity score matched with 40 patients treated with segmental transarterial chemoembolization combined with microwave ablation in a retrospective study of solitary HCC up to 3 cm.[7] The investigators found mRECIST complete response (CR) rates of 85.4% and 88.8% for RS and TACE-MWA, with a median follow-up in the RS group of 11 months and 20 months in the TACE-MWA group.[7] The same investigators also retrospectively compared RS vs segmental TACE alone (38 patients in each propensity score-matched group) and found CR rates of 92% vs 53% for RS and TACE, respectively, with median follow-up of 20 (RS) and 22 (TACE) months.[8]

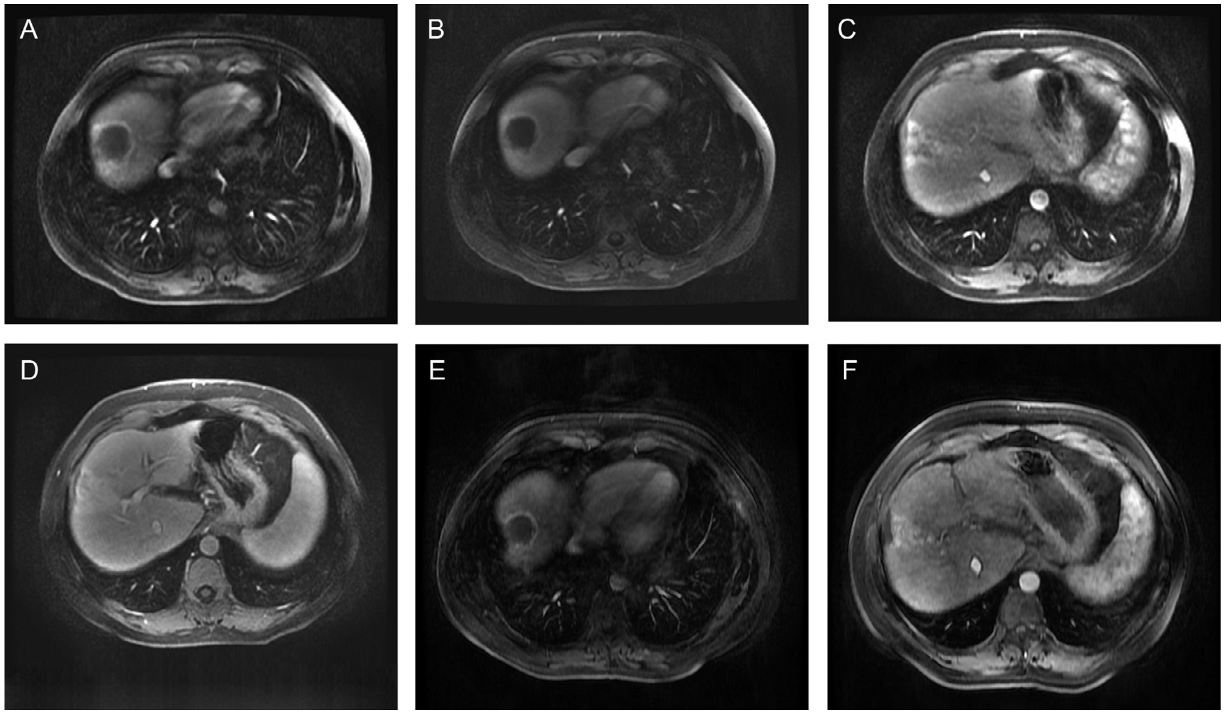

Figure 4 One- and 5-month postradiation segmentectomy MR images from patient treated in Figure 1. A. An arterial phase axial MR image through upper portion of treatment zone: only a rind of granulation tissue enhances along the margin of the treated tumor, while the tumor itself is completely nonenhancing. B. A portal phase image at same level shows the rim of enhancement persists, differentiating this from viable tumor; interior of tumor is darker than during portal phase of pretreatment scan (Figure 1b), consistent with necrosis. C. Arterial phase image through the lower portion of the treatment zone shows the typical wedge-shaped region of hyperenhancement containing areas of nonenhancing tissue. D. Portal phase image through the same level shows persistent hyperenhancement, not to be confused with progression of HCC. E, F. Five-month post-treatment arterial phase images show involution of the treatment zone—segmentectomy. The patient was subsequently transplanted. There was no viable tumor in the explant.

With a median follow-up of 11 months, another group of investigators reporting on a series of 101 radiation segmentectomies was recently reported with complete mRECIST imaging response in 92% and 84% of patients at 1 and 2 years follow-up, respectively, numbers typical of results from surgical resection.[9] Median tumor diameter was 3.2 cm.

Most recently, a series was reported of 70 patients with intact liver function treated with RS for HCC 5 cm or smaller.[10] With a mean follow-up of 29 months, patients had median overall survival of 6.7 years, and 1-, 3- and 5-year overall survival rates of 98%, 66%, and 57%, respectively, numbers again resembling those of curative-intent treatments like, resection, transplantation, and percutaneous thermal ablation. A subanalysis of patients receiving RS for HCCs 3 cm and smaller resulted in median 1-, 3-, and 5-year overall survival of 100%, 82%, and 75%, respectively. Notably, progression of disease usually occurred outside the treatment zone: local tumor control by EASL CR for the entire group at 5-year follow-up was 72%.

Adverse Events

In all published studies, RS has been shown to be safe or safer than segmental TACE or lobar TARE.[1,8-10] Toxicities were similar in the single study comparing RS with TACE-MWA.[7] Nontarget radioembolization, a rare but feared complication, is arguably less likely with RS, since radiomicrospheres are delivered more distally than with lobar treatment.

Radiation Lobectomy

RL was first described in 2009 as the occasional imaging finding of ipsilateral hepatic lobar atrophy and contralateral lobar hypertrophy after lobar TARE.[11,12] Since the initial reports of RL findings, there has been increasing interest in the potential to induce RL.

Indication/Clinical Evaluation

Beyond meeting the usual requirements for Y90 treatment, patients selected for RL will often have high performance status; unilobar, relatively small tumor burden; and intact or nearly intact liver function. RL can be performed as primary treatment or as a bridge to surgical resection with the aim of tumor ablation or instead of segmentectomy for somewhat larger or central tumors deriving supply from numerous arterial branches (Figure 5). RL shows promise in the reduction of portal vein tumor thrombus. In addition to its oncologic benefit, RL, can potentially be used instead of portal vein embolization (PVE) in patients with primary or oligometastatic hepatic malignancy who might

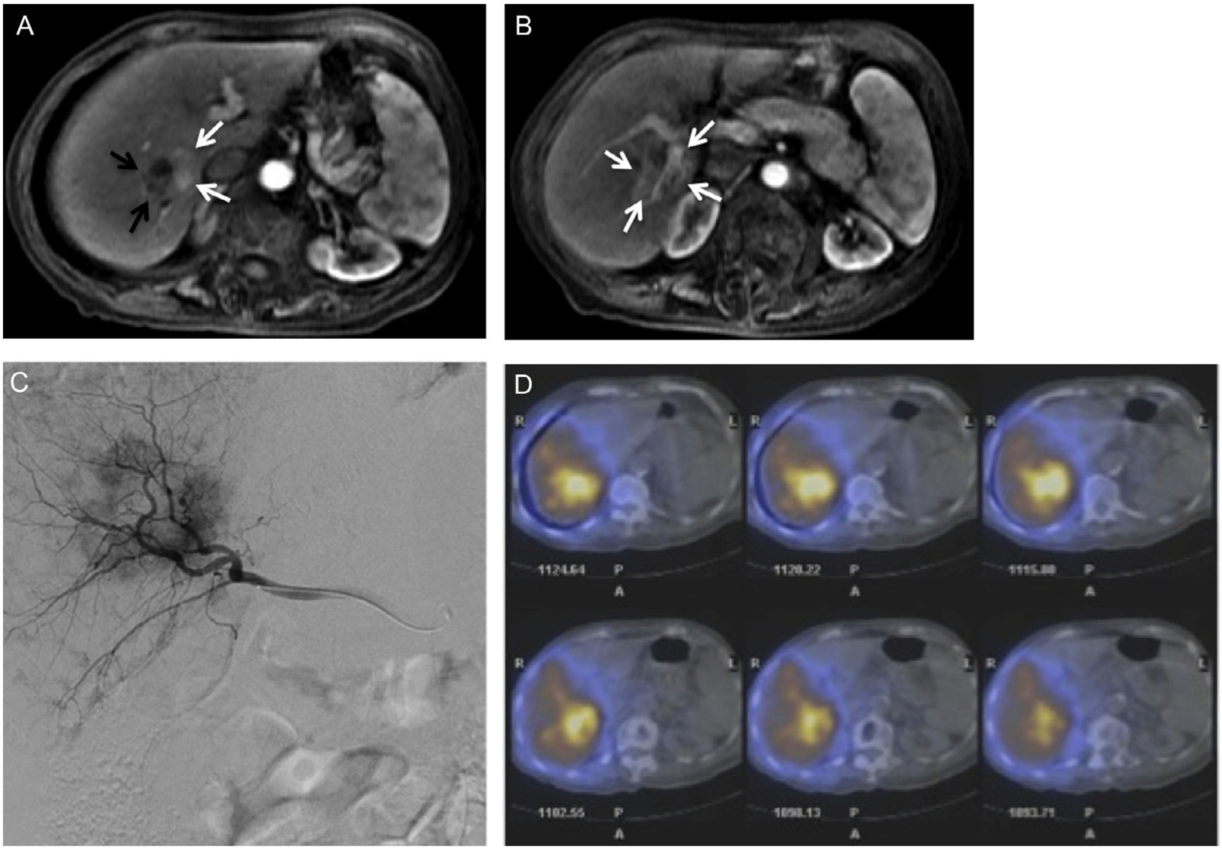

Figure 5 Lesion and treatment more commonly associated with radiation lobectomy. A. 4.0 cm diameter mixed HCC-cholangiocarcinoma on the deep margin of segments 6 and 7. The superior aspect of the tumor contains both cystic (black arrows) and solid, arterially enhancing (white arrows) components. The tumor abuts the adrenal gland (beneath the posterior white arrow). B. The inferior aspect of the tumor (white arrows) surrounds the posterior right portal vein. C. Distal right hepatic DSA demonstrates tumor blush and arterial supply from both anterior and posterior divisions. D. Serial axial SPECT images confirm intense radiotracer uptake by tumor (white-yellow) and less uptake throughout the rest of the right lobe (gray-orange). (Color version of figure is available online.)

benefit from lobar hepatectomy but who lack a sufficient volume of contralateral liver tissue, the future liver remnant (FLR).

Dosimetry and Angiographic Technique

As previously outlined, RL and radiation segmentectomy are off label indications supported by small but growing bodies of medical literature. Variations in the technique of RL are largely based on anecdotal evidence rather than published series.

To achieve RL using glass, many practitioners will increase the target MIRD dose from the conventional 120-140 Gy to 200 Gy. With resin, RL can be performed by targeting the lobar volume using as a minimum dose target the established tissue toxicity threshold of 70 Gy for cirrhotic liver or 80 Gy for noncirrhotic liver.[4] Using the 3 compartment partition model for resin lobectomy the tumor represents a nontarget sump.

Follow-Up and Expected Outcomes

If surgical hepatectomy is anticipated, post-treatment MR or CT volumetry can be obtained with routine post-TARE surveillance or at whatever interval best informs the decision to operate. Otherwise, clinical and imaging follow-up are identical to as after other radioembolization procedures.

A recent systematic review by Teo et al identified 7 retrospective single-center studies reporting degree of FLR hypertrophy associated with glass or resin RL.[13] Two hundred eighty-four of 312 patients received right lobe treatments. Two hundred fifteen, 12, and 85 of 312 patients had HCC, cholangiocarcinoma and metastases, respectively. The authors reported wide variation in the presence and severity of underlying liver disease, dosage and delivery of Y90, number of treatment sessions, and time to measurement of hypertrophy. Within the limitations of this heterogeneity, they found FLR hypertrophy of 26%-47% at a range of 1.5-9 months postradioembolization, a rate somewhat slower than that achieved by PVE or other methods. Typical RL imaging findings are depicted in Figure 6.

Two larger RL studies have been published to-date, one each using glass and resin radiomicrospheres, respectively.[14,15] Each of these groups reported a series of 83 patients with unilobar liver tumors comprised mainly of HCC (67 and 52 patients, respectively).

In the glass RL study, patients received right lobar treatment, even when segmental radioembolization was feasible, delivering a median of 112 Gy to the right lobe.[14] In this

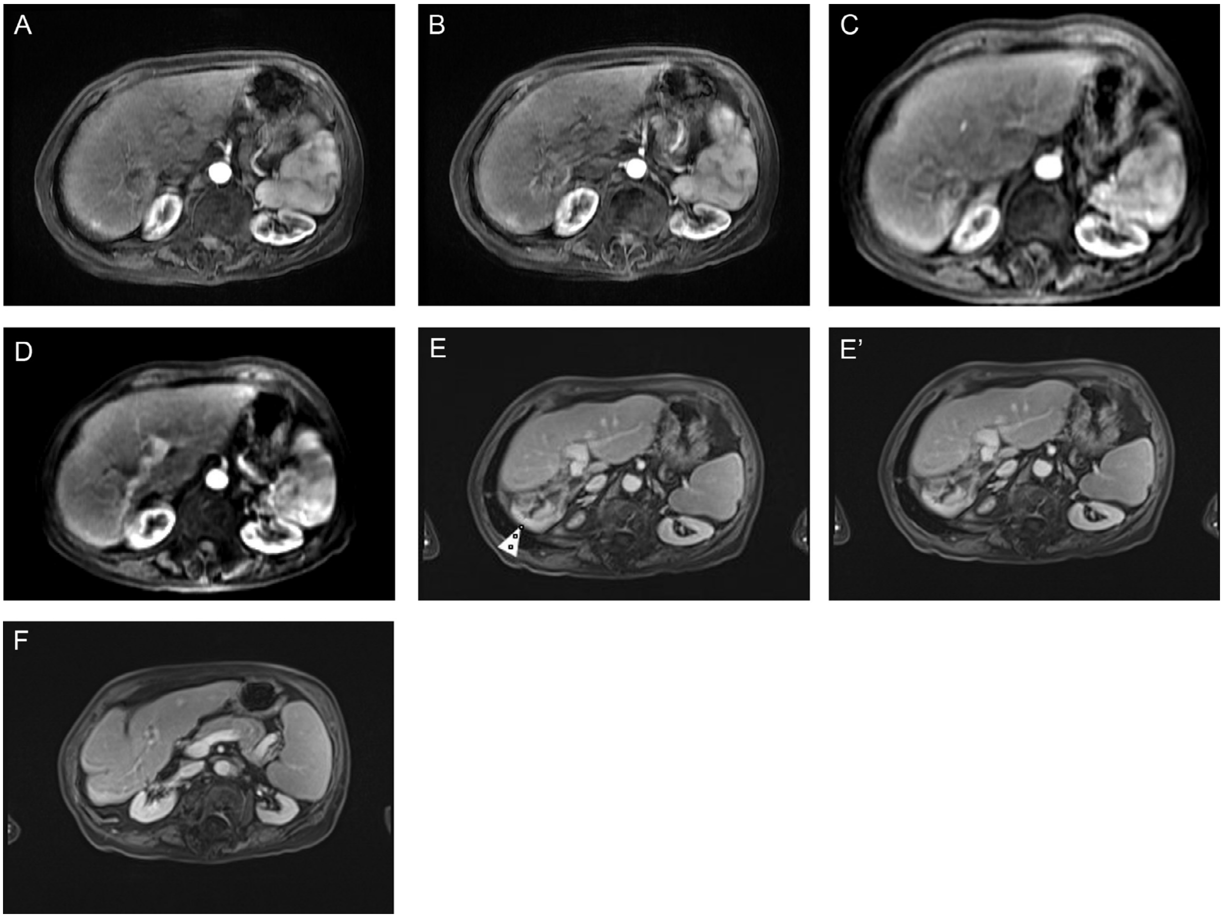

Figure 6 Typical radiation lobectomy findings. A and B. Arterial phase MRI through the superior and inferior aspects of the tumor treated in Figure 5, now 4 months after right lobe radioembolization, demonstrate decreased enhancement within the tumor, with a characteristic rim of persistent hyperenhancement. C and D. Twelve months after treatment there is marked atrophy of the right lobe and hypertrophy of the left lobe. The posterior right portal vein branch, previously surrounded by the tumor, remains patent. The tumor has decreased in size along with the rest of the lobe. Two years after treatment, the patient developed focal recurrence in the right lobe and was treated with stereotactic external beam radiotherapy. Six years after treatment, the patient remains alive and disease free. There has been near complete atrophy of the right lobe (white arrowhead) and the left lobe has grown to the size of the entire pre-treatment liver. The remaining right lobe is seen at the level of segments 4a and 2 (E), while segments 4b and 3 now occupy the entire space previously taken up by the whole liver (F).

series a median FLR hypertrophy of 45% was achieved at 9 or more months after delivery. Median tumor volume decreased from 134 to 56 mL after >9 months, and serum alpha fetoprotein levels in HCC patients decreased from 870 to 197 ng/mL. Median survival in Barcelona Clinic for Liver Cancer stage B and C patients was 34 and 9.6 months, respectively. Notably, most patients experiencing RL in this largest glass RL series had relatively small burden of disease: median tumor volume was 10% of right lobe volume, or 134 mL– the equivalent of a single spherical tumor 5.7 cm in diameter.[14] Patients also generally had intact liver function and performance status. Seventy-three of 83 patients (88%) in this study had ECOG PS of 0 or 1. Fifty-four, 34, and 12% of patients had Child A, B, and C cirrhosis, respectively.[14]

The authors of the largest resin RL series also reported a nearly 50% increase in FLR volume at 6 or more months follow-up.[15] They found a negative correlation between baseline bilirubin levels and degree of FLR hypertrophy. In reported results, there was no clear correlation between dose and degree of hypertrophy, delivered dose, tumor volumes, or oncologic outcomes.

Another series of 34 patients with HCC treated with glass RL was reported in which the investigators documented best tumor imaging response.[16] Delivering a median lobar dose of 122 Gy, response rates with RECIST 1.1 criteria were 0%, 26%, 63%, and 3% complete response (CR), partial response, stable disease and progression of disease, respectively. By mRECIST criteria, response rates were 30%, 33%, 30% and 2% CR, partial response, stable disease, and progression of disease. Median time-to-progression was 22 months, and median overall survival was 13.5 months. Eight patients progressed at 3 months follow-up due to development of new lesions, 3 of which were within the treated lobe.

A series of 52 patients with unilobar metastatic disease was reported comparing resin RL vs PVE in 26 pairs matched by baseline characteristics.[17] The majority of patients had received pre-RL platinum-based chemotherapy. Using BSA dosimetry, the investigators administered a median dose of 52 Gy to the lobe. The investigators found greater FLR hypertrophy with PVE than RL (62 vs 29%, $P < 0.001$) at a relatively short median follow-up time of 33 and 46 days for PVE and RL, respectively.

A series of 17 patients with right unilobar HCC treated with resin RL was reported in which it was found that patients with hepatitis B experienced significantly greater FLR hypertrophy than those with hepatitis C or alcohol-induced HCC (44 vs 8%, $P = 0.05$).[18] The authors posited that this difference was due to the absence of cirrhosis in the patients with hepatitis B.

Adverse Events

RL is well tolerated. Pain and nausea were common post-RL symptoms reported in the largest reported series of glass RL.[14] The investigators noted a slight worsening of Child-Pugh score from 6 to 7 in the first 6 months of follow-up which reversed at 6-9 month and longer follow-up. The authors of the largest published resin RL series found >20% average increase in splenic volume 6 or more months after treatment but no significant increase in rates of hypersplenism or additional radiologic findings of portal hypertension after treatment.[15] A statistically significant but clinically negligible increase in serum bilirubin was also noted, from 0.9 to 1.6 mg/mL through >26 weeks follow-up, without accompanying changes in prothrombin time or serum albumin levels.

Another study of resin RL reported 6 of 34 patients had serious toxicities, some being multiple.[16] These included 4 patients with temporary hyperbilirubinemia, 1 with progressive hyperbilirubinemia, 2 patients with reversible ascites, and 1 with irreversible ascites and variceal hemorrhage. Two of these 6 patients died.

Conclusion

While larger, comparative and, ideally, prospective studies must still be done, radiation segmentectomy is rapidly gaining wide acceptance as a safe, effective and potentially curative outpatient therapy. While published studies all describe RS using glass microspheres, the authors of this review and others do also provide RS using resin microspheres with anecdotally similar outcomes. Radiation lobectomy is another promising outpatient treatment option that may facilitate subsequent surgical hepatectomy or serve as destination treatment for those lacking surgical or thermal ablative therapeutic options.

References

1. Riaz A, Gates VL, Atassi B, et al: Radiation segmentectomy: A novel approach to increase safety and efficacy of radioembolization. Int J Radiat Oncol Biol Phys 79:163-171, 2011
2. Vouche M, Habib A, Ward TJ, et al: Unresectable solitary hepatocellular carcinoma not amenable to radiofrequency ablation: Multicenter radiology-pathology correlation and survival of radiation segmentectomy. Hepatology 60:192-201, 2014
3. Lau WY, Kennedy AS, Kim YH, et al: Patient selection and activity planning guide for selective internal radiotherapy with yttrium-90 resin microspheres. Int J Radiat Oncol Biol Phys 82:401-407, 2012
4. Garin E, Lenoir L, Edeline J, et al: Boosted selective internal radiation therapy with 90Y-loaded glass microspheres (B-SIRT) for hepatocellular carcinoma patients: A new personalized promising concept. Eur J Nucl Med Mol Imaging 40:1057-1068, 2013
5. Bilbao JI, Garrastachu P, Herraiz MJ, et al: Safety and efficacy assessment of flow redistribution by occlusion of intrahepatic vessels prior to radioembolization in the treatment of liver tumors. Cardiovasc Intervent Radiol 33:523-531, 2010
6. Mora RA, Ali R, Gabr A, et al: Pictorial essay: Imaging findings following Y90 radiation segmentectomy for hepatocellular carcinoma. Abdom Radiol 43:1723-1738, 2018
7. Biederman DM, Titano JJ, Bishay VL, et al: Radiation segmentectomy versus TACE combined with microwave ablation for unresectable solitary hepatocellular carcinoma up to 3 cm: A propensity score matching study. Radiology 283:895-905, 2017
8. Biederman DM, Titano JJ, Korff RA, et al: Radiation segmentectomy versus selective chemoembolization in the treatment of early-stage hepatocellular carcinoma. J Vasc Interv Radiol 29:30-37, 2018.e2
9. Padia SA, Johnson GE, Horton KJ, et al: Segmental yttrium-90 radioembolization versus segmental chemoembolization for localized hepatocellular carcinoma: Results of a single-center, retrospective, propensity score-matched study. J Vasc Interv Radiol 28:777-785, 2017.e1
10. Lewandowski RJ, Sato KT, Atassi B, et al: Radioembolization with 90Y microspheres: Angiographic and technical considerations. Cardiovasc Intervent Radiol 30:571-592, 2007
11. Gaba RC, Lewandowski RJ, Kulik LM, et al: Radiation lobectomy: Preliminary findings of hepatic volumetric response to lobar yttrium-90 radioembolization. Ann Surg Onc 16:1587-1596, 2009
12. Siddiqi NH, Devlin PM: Radiation lobectomy—A minimally invasive treatment model for liver cancer: A case report. J Vasc Interv Radiol 20:664-669, 2009
13. Teo J-Y, Allen JC Jr., Ng DC, et al: A systematic review of contralateral liver lobe hypertrophy after unilobar selective internal radiation therapy with Y90. HPB 18:7-12, 2016
14. Vouche M, Lewandowski RJ, Atassi R, et al: Radiation lobectomy: Time-dependent analysis of future liver remnant volume in unresectable liver cancer as a bridge to resection. J Hepatol 59:1029-1036, 2013
15. Fernandez-Ros N, Silva N, Bilbao JI, et al: Partial liver volume radioembolization induces hypertrophy in the spared hemiliver and no major signs of portal hypertension. HPB 16:243-249, 2014
16. Edeline J, Lenoir L, Boudjema K, et al: Volumetric changes after 90Y radioembolization for hepatocellular carcinoma in cirrhosis: An option to portal vein embolization in a preoperative setting? Ann Surg Onc 20:2518-2525, 2013
17. Garlipp B, de Baere T, Damm R, et al: Left-liver hypertrophy after therapeutic right-liver radioembolization is substantial but less than after portal vein embolization. Hepatol 59:1864-1873, 2014
18. Teo JY, Goh BKP, Cheah FK, et al: Underlying liver disease influences volumetric changes in spared hemiliver after selective internal radiation therapy with 90Y in patients with hepatocellular carcinoma. J Dig Dis 15:444-450, 2014